NIH HEAL
EPPIC-Net
Early Phase Pain Investigation
Clinical Network
Applicant Webinar
August 23, 2019

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NIH/NINDS
barbara.karp@nih.gov
For clearest audio, please mute your microphone.

Please note that the webinar is public and is being recorded.

The webinar recording will be posted on NIH websites and will be available for later viewing.

Please save all questions for the end.
  - You can e-mail questions to the speakers during the webinar or use Q&A panel or the "chat" feature on Webex.

The purpose of the webinar is to provide information on the asset application submission and review process.

Please do not ask about specific assets or applicants during the webinar. Questions about specific assets or studies can be emailed to EPPIC-Net staff.
EPPIC-Net Asset Applicant Webinar: Agenda

• Welcome and introductions- Barbara I. Karp, MD, EPPIC-Net Program Director
• Welcome and HEAL Initiative introduction- Rebecca Baker, PhD, Director, NIH HEAL Initiative
• EPPIC-Net Overview, purpose
• Infrastructure
• Asset solicitation
• Application overview
• Funding information
• Preliminary application guide
• Review process – Marilyn Moore-Hoon, PhD; SRO NINDS
• eRA Commons – Laurie Roman, PhD, MBA; NIH/OD/OER/ORIS/eRA
• Q and A – all presenters
NIH HEAL (Helping to End Addiction Long-term) Initiative

Rebecca G. Baker, Ph.D.
Director, HEAL Initiative, Office of the Director, National Institutes of Health
• Trans-NIH research initiative to:
  • Improve prevention and treatment strategies for opioid misuse and addiction
  • Enhance pain management
• Goals are scientific solutions to the opioid crisis
• Coordinating with the HHS Secretary, Surgeon General, federal partners, local government officials and communities

www.nih.gov/heal-initiative
$500M/year Trans - NIH effort
  • Over $850M to be obligated in FY2019
12 NIH Institute and Centers leading 26 HEAL research projects
  • Over 20 collaborating Institutes, Centers and Offices
  • From prevention research, basic and translational research, clinical trials, to implementation science
  • Multiple projects integrating research into new settings
Released 40+ funding announcements for FY2019
HEAL Initiative Research Overview

Enhancing Pain Management

- Pre-Clinical Research in Pain Management
- Expand Therapeutic Options
- Develop New/Improved Prevention & Treatment Strategies
- Optimize Effective Treatments
- Clinical Research in Pain Management
- Enhance Treatments for Affected Newborns

Improving Treatments for Misuse and Addiction
Enhancing Pain Management

- **Clinical Research in Pain Management**
  - Characterize populations of patients with pain conditions
  - Test novel treatments in a new clinical trials network
    - Early Phase Pain Investigation Clinical Network (EPPIC Net)
    - Back Pain Research Consortium
  - Establish best strategies for management of acute and chronic pain
    - Pain Management Effectiveness Research Network
    - Integrated approach to pain and opioid use in hemodialysis patients
    - Pragmatic and Implementation Studies for the Management of Pain
NIH HEAL
EPPIC-NET

Barbara Illowsky Karp, M.D.
Program Director: EPPIC-Net
National Institutes of Neurological Disorders and Stroke
National Institutes of Health
HEAL Programs for Pain

Discovery
- Acute to Chronic Pain Signatures
- Discover and Validate Novel Targets

Preclinical Development
- Preclinical Screening Platform
- Small Molecules and Biologics Development
- Device Development

Clinical Trials
- Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints

Implementation/Dissemination
- Data & Asset Sharing Partnership
- Early Phase Pain Investigation Clinical Network
- Back Pain Research Consortium
- Hemodialysis Pain Management
- Pain Effectiveness Research Network
- Pragmatic and Implementation Studies for the Management of Pain
The goals of EPPIC-Net are to provide academic and industry investigators with expert infrastructure and support for early-phase clinical testing of pain therapeutics across populations and the lifespan AND to reduce reliance on opioids by accelerating early-phase clinical trials of non-addictive pain therapeutics, including drugs and devices.
EPPIC-Net Overview

EPPIC-Net will:

- Test new pain treatments (compounds and devices judged highly meritorious in peer review that come from industry and academia) in early-stage trials
- Incentivize, accelerate Phase II trials; Reduce the time to start, enroll, run, and complete trials
- Focus on well-defined pain conditions with high-unmet need; provide well-characterized pain patient cohorts for EPPIC-Net clinical trials, incorporating deep phenotyping
- Provide proof-of-concept testing of potential biomarkers and new non-addictive treatments
- Validate biomarkers for utility in assessing target engagement or pain outcomes
- Develop and test innovative clinical trial paradigms to engineer adaptive, ever-improving early-phase testing of new pain therapies
EPPIC-Net is collaborating with the NIAMS Back Pain Consortium (BACPAC) Research program. BACPAC is focused on chronic low back pain research using novel, inter- and multidisciplinary integrated approaches and novel analytics for discovery of disease mechanisms and features for deep patient phenotyping and identification of new targets for intervention.

More information can be found in the following notices:

EPPIC Network Advantages

• Increased trial quality
• Balanced portfolio
  – Allows logical ordering of incoming trials
  – Creates a pipeline for future trials
• Stable infrastructure and research capacity
  – Stable funding for research and training
• Required data sharing
  – Single data center with uniform governance and quality assurance
  – Use of CDEs within EPPIC-Net and within HEAL
  – Data will be submitted to central HEAL data repository for broad use/sharing
• Biosample repository and sharing
• Manages trials competing for similar patients
• Coordinates with non-profits, industry, and international partners
• Trains the next generation of clinical trialists
EPPIC NET – Infrastructure Defined

**Clinical Coordinating Center (CCC)**
- Manages centralized IRB arrangements and Master Trial Agreements
- Match Hubs/Spokes to the protocol/asset
- Identify and train site investigators/staff
- Standardize CRFs, CDE’s and methodologies
- Work with DCC; develop SOPs and quality controls
- Distribute funds with NINDS oversight

**Data Coordinating Center (DCC)**
- Receives, processes and centralizes data
- Provide statistical/analysis reports
- Harmonizes with data from other HEAL studies
- Monitors safety/provides reports to DSMB and other monitors
- Creates data repository; Manages EPPIC-Net data
- Biorepository for EPPIC-Net and other HEAL projects

**Clinical Hubs & Spokes**
- Identifies individual investigators
- Conducts trials
- Collects and reports data to DCC and CCC

**NIH**
- Selects Assets for study
- Interacts with all EPPIC-Net components
- Provides oversight of studies
- Oversees budget and milestones

**Funding for infra-structure components are U24 Cooperative Agreements.**
Those from Industry, Academia (and Elsewhere) are invited to submit applications for assets to be studied within EPPIC-Net

- EPPIC-Net is seeking non-addictive therapeutics for targeted pain conditions that currently lack adequate treatment

- Drug, biologics, and device assets considered

- All pain conditions considered

- Studies addressing pain across the age spectrum encouraged

- Assets that serve for proof-of-concept testing considered

- Re-purposed drugs considered

- Phase 2 ready with existing IND/IDE desirable

- The asset and IP remain the property of the asset owner; Confidentiality agreements implemented as needed. Technology transfer agreement (CRADA or other) defines relationship between EPPIC-Net and asset owner.
EPPIC NET – 3 stage application process

Each stage requires separate submission.

Stage 1
- Preliminary application submission and review

Stage 2
- Dossier preparation, submission and review

Stage 3
- Protocol preparation, submission and review

- Protocol Funding Award
- Assignment to Clinical Sites
- Implementation
EPPIC-Net Application Overview

Asset (drug/device) proposed by applicant

Objective review #1

Objective review #2

Objective review #3

Clinical Coordinating Center

Clinical trial protocol development

Clinical trial conducted

Preliminary application

Dossier Application (invitation only)

Protocol Application (invitation only)

Eventual Phase III clinical trial pursued by company outside of EPPIC-Net
**EPPIC NET – Funding information**

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<thead>
<tr>
<th>WHAT:</th>
<th>WHO:</th>
<th>AWARD:</th>
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<tbody>
<tr>
<td>Preliminary Asset Application</td>
<td>Brief Asset Data</td>
<td>Applicant</td>
</tr>
<tr>
<td>In Depth Asset Review: Dossier</td>
<td>Complete Asset Dossier</td>
<td>Applicant and NINDS Contractor</td>
</tr>
<tr>
<td>Clinical Trial Protocol review</td>
<td>Clinical Trial Protocol</td>
<td>EPPIC-Net CCC* (with DCC, Hub PIs and Applicant)</td>
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**Objective Review Panel**
Evaluates assets based on preliminary application, dossier, and clinical protocol

**MDWG** **NINDS Council** **NIH HEAL Executive Committee**

"Other Transaction" (OT) Awards are used to fund EPPIC-Net Clinical Trials

*OT award made to CCC for distribution to Hubs/spokes for trial conduct. Asset owner does not receive funds; Asset holder gains access to EPPIC-Net for asset clinical trial."
EPPIC-Net Preliminary application packet is available at


Preliminary application packet includes

1. Information sheet with contact addresses
2. Preliminary application (fillable .pdf)
3. Line-by-line application instructions
4. eRA Commons submission instructions
EPPIC-NET Preliminary Application

- Applicant information
- Asset information
- Freedom to operate
- Biological rationale
- Relevant prior studies (preclinical and clinical) with relevant literature citations
- Proposed indication
- Proposed treatment regimen
- Proposed outcome measures (efficacy, biomarkers, and safety)
- FDA/regulatory status
- Feasibility/logistics concerns
Applications selected through rigorous review process will work with an NIH contractor to prepare the Stage 2/Dossier application.

- Scientific rationale
- Clinical unmet need
- Target product profile (TPP)
- Target-disease connection
- Preclinical Data Package
- Chemistry/manufacture, device specifications
- Biology, pharmacology, physiology
- Clinical data to support proposed trial
- Clinical considerations for HEAL Program
- Non-scientific considerations
EPPIC-NET Protocol Application

Dossier applications selected through rigorous review process will work with EPPIC-Net infrastructure (led by CCC) to prepare the Stage 3/Protocol application

- Protocol will be based on NIH/FDA template
- Full trial information and plan
- Human subjects protections addressed
- Stage 3 application includes proposed budget and study timeline
- Stage 3 applicant is CCC in coordination with asset owner
EPPIC-Net Review process and criteria

Marilyn Moore-Hoon, PhD
Scientific Review Officer
NINDS
Objective Reviews are NOT using the standard NIH Peer Review process!!!
# EPPIC NET – Review process and criteria

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**Objective Review Panel**
Evaluates assets based on template, full dossier, and clinical protocol

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- NIH IC Staff
- HEAL MDWG
- NINDS Council
- NIH HEAL Executive Committee
Goals of Objective Review

• To get expert input for NINDS/HEAL consideration of EPPIC-Net awards
• To have a fast, streamlined review process
• To get reviewers’ individual opinions on each proposed therapeutic.
  • Consensus is *not* the goal. Scores will *not* be stated out loud at the meeting or averaged after the meeting – each reviewer’s score stands alone.
• Conflicts of Interest (COI) will be managed using standard review COI policy as a guide.
Objective Review Panel Composition

• 25-30 Core panel members. Same panel for all stages of review (different members may be present)

• Expert ad hoc reviewers as needed to cover science, rigor, and methodology

• As a therapeutic moves through the application stages – stage appropriate expertise will be included.
EPPIC-NET EPPIC NET Preliminary Application

Review Timeline

- Review of applications for all stages should be completed within 2 months of receipt.
- Applications are submitted on a rolling basis: meeting cut-off dates will be posted on the EPPIC-Net webpage:
  - e.g. “All applications received by Oct 1 will go to review at the end of Oct meeting.”
- Applicants will be notified of the outcome, but **NO** Summary Statements provided
  - Feedback will focus on therapeutics of interest
Application Review

Pre-meeting individual reviewer assessment will identify 3-4 key strengths and weaknesses and an initial recommendation for a color “Bin”:

- **GREEN** – Meritorious – will be discussed
- **YELLOW** – Meritorious, but concerns noted – may be discussed
- **RED** – Not deemed meritorious – will not be discussed.
Stage 1 Review Criteria

- Significance
- Approach
- Viability/Feasibility
Significance

• Do the asset and approach appropriately target a specific type of pain with high unmet therapeutic need?

• Do the asset and approach represent a marked improvement over existing pain therapies?

• Will the asset and proposed study notably advance the field of pain therapy?
Approach

- Is the strategy for testing this asset in a Phase 2 Clinical Trial realistic?
- Will the asset be scalable?
  - Are there plans to have enough asset available for a Phase 2 Clinical Trial?
  - Will the asset be scalable for eventual clinical use?
- Is there a reasonably rapid timeline for bringing this asset to a clinical trial?
- Are novel methods, assays, or approaches proposed?
- Are safety and biohazard considerations for use of the asset in humans clearly addressed?
Viability/Feasibility

• Is the asset appropriate for the proposed indication?
• Does the study information provided, support a Phase 2 Clinical Trial?
• Is there a path forward for eventual clinical adoption?
• Are there barriers to use of the asset in the proposed study or eventually in the clinic?
• Have safety and regulatory IND/IDE studies been completed, indicating readiness for a Phase 2 Clinical Trial?
Stage 2 and 3: Objective Review

- Same Objective Review panel with additional ad hocs for proper science and stage evaluation.

- Different criteria matched to stage of review

- Stage 3 will be similar to an NIH standard review to ensure consideration of required policies such as *The Protection of Human Subjects* and *Inclusion Across the Lifespan*. 
EPPIC-Net eRA Commons

Laura M. Roman, MBA, PhD
eRA/OER
eRA Commons

Registrations

• Submitting organization must be registered at eRA Common
• Organization must have individual with role of Signing Official
• Streamlined Commons registration process: no DUNS required for submission
• PD/PI must have Commons ID and be affiliated with submitting organization
EPPIC-Net: Preparation, Submission & Tracking

Application Preparation & Submission in ASSIST

- NIH’s System to System solution
- Application preparation, submission & tracking in a single system
- Streamlined submission - single form + attachments
- Use opportunity provided in EPPIC-Net (OTA-XX-XXX)
- if PI completes profile in eRA Commons, can use Commons ID to prepopulate select fields
EPPIC-Net: Preparation, Submission & Tracking

Enter opportunity announcement # here*

*Research Opportunity Announcement (ROA) # will be posted on EPPPIC-Net website on Sept 3

Enter title for application
EPPIC-Net: Preparation, Submission & Tracking

Application Information

- **Application Identifier:** 21115
- **Application Project Title:** Clinical Center for All of Us NIH Program
- **PD/PI Name:** AARONS, GREGORY
- **Organization:** 
- **Project Period:** 
- **Status:** Ready for Submission
- **Status Date:** 2018-05-16 10:50:09.000 PM EDT
EPPIC-Net: Preparation, Submission & Tracking
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### ASSIST

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### Agency

**View Agency Submission Errors and Warnings**

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2019

Preliminary application submission and review

September

Dossier preparation, submission and review

October

Protocol preparation, submission and review

November

December

2020

FUNDING AND IMPLEMENTATION OF FIRST TRIALS

February

January
EPPIC-Net opens for applications on **Sept 3, 2019**. Please check the website for updates, the ROA # needed to complete the application, and to join the EPPIC-Net list-serv.

### EPPIC-Net Contacts:

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**EPPIC-Net Program Assistant**  
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### HEAL Contacts:  
https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative

### eRA Commons Contacts:  
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THANK YOU FOR YOUR INTEREST IN NIH HEAL AND EPPIC-NET